EXHIBIT C

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION **THIS DOCUMENT RELATES TO ALL WAVE 1, 2, and 3 Cases**	**Master File No. 2:12-MD-02327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

SUPPLEMENTAL RULE 26 EXPERT REPORT OF JERRY G. BLAIVAS, M.D.

The following supplemental report is provided pursuant to Rule 26(e)(2) of the Federal Rules of Civil Procedure. This supplemental report provides additional support that was not previously available for some of my opinions in my January 28, 2016 expert reports (collectively referred to herein as "report" or "expert report") provided in the Ethicon Wave 1, 2 and 3 cases.

1. In my report, I opined that the Gynecare TVT family of devices causes serious and life-style altering complications. These opinions are supported by recent peer reviewed literature. For example, in an article published in April 2016[1], the authors noted that "certain complications from MUS surgery are unique to the use of polypropylene mesh. These can include mesh exposure, chronic pelvic pain, and dyspareunia, which are the most common, as well as mesh contracture, organ perforation, and/or neuromuscular injury. Other complications may include *de novo* urgency and/or urgency urinary incontinence (UUI), urinary tract infection (UTI), and/or urinary obstruction." These conclusions are consistent with and provide further support for the opinions in my original report.

2. New articles also report complication rates associated with MUS that are consistent with those reported in my publication in Nature referenced in the report and may be higher than originally believed. For example, Brown et al. report an overall sling revision rate of 2.7% with "the following indications: urinary retention (43.8 %), voiding dysfunction (42.7 %), recurrent UTI (20.2 %), mesh erosion (21.3 %), vaginal pain/dyspareunia (7.9 %), and groin pain (3.4 %)." (*Id*.) Dr. Brown and colleagues likewise concluded that "a tertiary care, multicenter, retrospective analysis also reported complications from MUS to be quite high . . . Overall, these complication rates shown in the TOMUS trial are much lower than those reported by

[1] Timbrook Brown E, et al., Evaluation and management of mid-urethral sling complications, Curr. Bladder Dysfunct. Rep., 2016 Apr 18: 1-9.

the more recent retrospective studies, suggesting that com-plication data in a RCT can be limited. As such, we can extrapolate from the current studies that the overall complication rates are higher than originally reported and a lack of consistent follow-up with the initial surgeon may contribute to this." (*Id.*) These conclusions are consistent with and provide further support for the opinions in my original report.

3. In my report, I opined that many of these complications cannot be easily managed. Since that time, additional peer reviewed literature has been published that further supports my opinions. In the Brown paper, the authors note that "Unfortunately, despite multiple attempts at surgical revision, complications from MUS can be quite morbid." Dr. Brown and his colleagues cautioned surgeons regarding mesh implants that they needed "a high index of suspicion for intraoperative and post-operative complications" and also noted that "[t]he overall rate of MUS complications is difficult to ascertain as there are limited randomized controlled trials (RCTs) with adequate follow-up - - many complications can present much later than the defined study period." (*Id.*) These conclusions are consistent with and provide further support for the opinions in my original report.

4. In my report, I opined that pain and dyspareunia from MUS are considerably greater and lasts longer than routine post-operative pain and treatment is extremely challenging. I also offered the opinion that the pain may continue, or even worsen, after mesh excision or revision. Recently, Brown et al. stated that "Vaginal and/or pelvic pain, associated with or without dyspareunia, can be a quite difficult clinical presentation to evaluate and manage . . . Unfortunately, MUS excision may not be curative and debilitating pain can still result." (*Id.*) These conclusions are consistent with and provide further support for the opinions in my original report.

5. I also opined that the pubovaginal sling is a safe and effective alternative to the Gynecare polypropylene midurethral slings. Additional evidence supports my opinions. In 2016, the working group for the International Federation of Gynecology and Obstetrics published an abstract in the Journal of Neurourology Urodynamics.[2] The group concluded, as have I in my original report, that the pubovaginal sling, the Burch colposuspension, and midurethral slings, are all effective treatments for stress urinary incontinence ("SUI"). (*Id.*) Similarly, in an article appearing in Research and Reports in Urology, the authors addressed "the various aspects of autologous PVS and its indications as an alternative to synthetic slings." They concluded that the "autologous PVS is an effective and safe option for surgical treatment of primary and secondary SUI. It can be safely performed with a low morbidity rate and a negligible erosion risk in comparison to synthetic slings."[3] Finally, in an abstract published in 2016 in the American Journal of Obstetrics and Gynecology,[4] the authors concluded that "[t]his nationwide cohort study provides physicians with a representative evaluation of the rate of reoperations after surgical procedures for urinary incontinence. Pubovaginal slings, Burch

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[2] Medina CA, et al., Evaluation and surgery for stress urinary incontinence: A FIGO working group report, Neurourol. Urodyn., 2016 Mar 7.

[3] Bang, et al., Autologous pubovaginal slings: back to the future or a lost art? Research and Reports in Urology, 18 Jan 2016, Vol. 216:8, pg. 11-20.

[4] Foss et al., Reoperation for urinary incontinence: a nationwide cohort study, 1998-2007, Am J Obstet Gynecol, Feb. 2016.

colposuspension, and retropubic midurethral tape had a similar risk of reoperation (6%). (*Id*.) Women who were operated with transobturator tape had a significantly higher risk of reoperation compared with retropubic midurethral tape." (*Id*.) These findings are consistent with my opinions and provide further support for them.[5]

6. In my original report, I opined that the polypropylene mesh in the Ethicon MUS can cause chronic inflammation and/or degrade *in vivo*. This opinion has been further supported by new peer reviewed literature. Nolfi et al. published a study in the American Journal of Obstetrics and Gynecology entitled "Host Response to Synthetic Mesh in Women with Mesh Complications."[6] In that study, the authors examined the explanted vaginal tissue of 27 women who had received either a polypropylene midurethral sling or a polypropylene mesh device for the treatment of their pelvic organ prolapse ("Prolapse" or "POP"). The authors concluded that a "persistent foreign body response was observed in mesh tissue complexes excised from women requiring surgical excision of mesh months to years after mesh implantation." (*Id*.) The authors also concluded that "[i]mportantly, the presence of macrophages was limited to the area immediately surrounding the mesh fibers with each fiber eliciting an independent reaction, the magnitude of which appeared to be proportional to the number of fibers in a given area. This points to the importance of maintaining meshes in a flat (as opposed to folded) configuration to minimize the amount of material per area and choosing meshes in which the spaces between fibers (pores) are wide enough that the host response to two adjacent fibers does not overlap." (*Id*.) Notably, the authors also stated that the "Gynemesh PS has a highly unstable geometry when loaded, resulting in pore collapse and increasing stiffness of the product. Mesh deformation (contraction, retraction, or shrinkage) is also frequently observed in meshes removed for pain." (*Id*.) The authors also concluded that the "increase in MMP-9 in mesh explants that were removed for exposure indicates degradation; the positive association between interleukin-10 and M2 macrophages in mesh explants that are removed for pain in consistent with fibrosis." (*Id*.) These conclusions are consistent with the opinions offered in my original report and provide additional support for those opinions.

7. Additional new literature also supports my opinion that mesh degrades *in vivo*. In an article published in Biomaterials entitled "*In vivo* oxidative degradation of polypropylene pelvic mesh,"[7] the authors found that the

> "overall degradation process of PP pelvic meshes may be summarized as follows. The implant causes increased activity by oxidative enzymes in the vicinity of the implant. This leads to an oxidative degradation process that is evidenced by appearance of hydroxyl and then carbonyl groups in the polypropylene, as observed

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[5] *See also* Mock, et al., Contemporary Comparison between Retropubic Midurethral Sling and Autologous Pubovaginal Sling for Stress Urinary Incontinence after the FDA Advisory Notification *Urology 2015; 85: 321-325 (*" In this contemporary cohort of women considered suitable candidates for either a PVS or an MUS, both offer comparable efficacy and complication rates. PVS may be safely offered to patients who would otherwise be good candidates for MUS if they are concerned with the implantation of mesh.") (Abstract)

[6] Nolfi AL, et al., Host Response to Synthetic Mesh in Women with Mesh Complications, Am J Obstet Gynecol 2016; 215:206.e1-8

[7] Imel, Adam, et. al, *In vivo* oxidative degradation of polypropylene pelvic mesh, Biomaterials 73 (2015) 131-141, 10.1016/j.biomaterials.2015.09.015

> by infrared spectra. There is accompanying degradation of the polypropylene molecular weight, and this process may be delayed, but not prevented, by the presence of antioxidants in the polypropylene. Antioxidants are preferentially consumed by the oxidizing species and finally the concentration falls below a level required to protect the polymer and oxidative degradation occurs. This degradation is accompanied by a decrease in mechanical properties (embrittlement, loss of mass, decreased melting temperature, reduced compliance) of the polypropylene. In particular, the surface and amorphous regions of the polypropylene are selectively degraded, resulting initially in cracks and, on longer exposure, fragmentation of the implant.

(*Id.*)

These conclusions are consistent with and provide further support for the opinions in my original report.

8. In addition, newly-published animal studies also support my opinions. The American Journal of Obstetrics and Gynecology published a study entitled "Characterization of the host inflammatory response following implantation of prolapse mesh in rhesus macaque."[8] In that study, the authors concluded that their "findings correlate with those of a previous study demonstrating that lighter-weight, higher-porosity mesh was also associated with fewer negative effects on vaginal tissue quality. This suggests that the chronic M1 pro-inflammatory response to mesh may drive tissue degradation eventually leading to mesh exposures over time similar to what is observed clinically; however, additional work is required to establish a causal relationship." (*Id.*) These conclusions are consistent with and provide further support for the opinions in my original report.

9. Likewise, in an article published in the Journal of Biomedical Materials,[9] the authors studied 164 excised meshes "to search for features of polypropylene degradation" and concluded that "polypropylene degradation can be detected by readily available conventional light microscopy. A number of features indicated that polypropylene degrades while in the body." These conclusion are consistent with and provide further support for the opinions in my original report.

This 17th day of October, 2016.

Jerry G. Blaivas, MD

[8] Brown et al., Characterization of the host inflammatory response following implantation of prolapse mesh in rhesus macaque, Am J Obstet Gynecol (2015), doi: 10.1016/j.ajog.2015.08.002

[9] Iakovlev V., et al., Degradation of polypropylene in vivo: A microscopic analysis of meshes explanted from patients. J Biomed Mater Res Part B 2015:00B:000